REMARKS

This amendment is submitted in response to the Office Action mailed November 13, 2007, in connection with the above-identified application (hereinafter, the "Office Action"). The Office Action provided a three-month shortened statutory period in which to respond, ending on February 13, 2008. Accordingly, this amendment is timely submitted.

I. Pending Claims

Claims 1-13, of which claims 1 and 13 are independent, remain pending. New claims 49-50 are added. No new matter is presented in the newly presented claims. Claims 10-12 and 14-48 are canceled. Applicants reserve the right to pursue the canceled claims in a divisional or continuation application. Applicants do not acquiesce in the correctness of the rejections or objections in the Office Action and reserve the right to present specific arguments regarding any rejected or objected-to claims not specifically addressed. Further, Applicants reserve the right to pursue the full scope of the subject matter of the claims in a subsequent patent application that claims priority to the instant application.

Independent claim 1, as amended, is now drawn to a method for up regulating runt-related transcription factor 3 (RUNX3) expression in a subject whereby an active agent is delivered to the immune cells of a subject that has a low activity or no activity of RUNX3 gene product. The active agent, in turn, induces expression or over-expression of RUNX3 in the immune cells of the subject, thereby inhibiting T cell proliferation in the subject. Support for the amendments is found in the entire specification, particularly at page 7, paragraphs [0084]-[0088], Examples 1-6, and Figures 1-6.

Independent claim 13, as amended, is now directed to a method for reducing the proportion of mature dendritic cells versus immature dendritic cells in a subject by delivering an active agent to the immune cells of a subject that has a low activity or no activity of runt-related transcription 3 factor (RUNX3) gene product, wherein the active agent induces expression or over-expression of RUNX3 in the immune cells of the subject, such that the proportion of mature dendritic cells versus immature dendritic cells in the subject is reduced. Support for this amendment is found throughout the entire specification, particularly at pages 6-7, paragraphs [0081-0085], and Examples 5-7.

To correct a minor clerical error, a comma (,) has been inserted after the transitional phrase in claims 2-4 and 8-9. In addition, the article "the" has been substituted with the term "said" in claims 1-8 and 13.

New claims 49-50, which are both dependent on claim 13, are added to further illustrate the claimed invention. Support for this amendment is found in the specification, particularly at page 2, paragraphs [0022] and [0034]; page 7, paragraph [0081]; and page 11, paragraphs [0122] and [0123].

New claim 51, which is dependent on new claim 50, recites that the polynucleotides further comprise a viral-based vector. Support for this amendment is found in the specification, particularly on paragraphs [0086].

Applicants respectfully submit that the rejections based on lack of enablement is overcome in view of the amendments and arguments presented in the response herein. Applicants hereby request that all amendments be entered at this time and reconsideration of this application be made in view of the above amendments and the following remarks.

IV. Rejection Under 35 U.S.C. § 112, First Paragraph

On pages 2-11 of the Office Action, the Examiner has maintained the rejection of claims 1-9 and 13 under 35 U.S.C. §112, first paragraph, for lack of enablement. In particular, according to the Examiner the "specification fails to enable the claimed methods for treating a T-cell mediated inflammation or attenuating dendritic cell maturation in vivo by way of the claimed methods," which "would required undue experimentation to make and use the claimed invention without a reasonable expectation of success." Applicants respectfully traverse the rejection in light of the remarks presented hereinbelow.

Independent claim 1, as amended herein, is now directed to a method for up regulating RUNX3 expression in a subject that includes delivering an active agent to an immune cell of the subject having low activity or no activity of RUNX3 gene product, wherein the active agent induces expression or over-expression of RUNX3 in the immune cells of the subject, thereby inhibiting the proliferation of T-cells. As illustrated in the Examples and Figures 1-6, Applicants respectfully submit that amended claim 1, as well as the claims that depend therefrom (claims 2-9) are enabled.

Dependent claim 2 recites that the immune cells are thymocytes or dendritic cells. Support for this claim is found in paragraphs [0022] and [0034] and page 11, paragraphs [0122-0123] of the specification.

Dependent claim 3 recites that the immune cells are dendritic cells. Support for this claim is found at pages 6-11 of the specification, as well as the corresponding Examples and Figures.

Dependent claim 4 recites that the active agent reduces the proportion of mature dendritic cells versus immature dendritic cells. Support for this claim is found throughout the entire specification and Examples 5-7.

Dependent claim 5 recites that reduction in the proportion of the mature dendritic cells versus immature dendritic cells can be determined by a reduction in the proportion of dendritic cells expressing CD80, CD86, MHC and OX40L. Support for this claim is on page 7 and Example 6 of the specification.

Dependent claims 6-7 recite that (1) the active agent is selected from the group consisting of a polynucleotide encoding RUNX3 and a polynucleotide encoding a RUNX3 promoter activator; and (2) that the polynucleotide further comprises a viral based vector. Support for these claims is found on paragraph [0086] of the specification.

Dependent claim 8 recites that the delivery step is performed *ex vivo*. Support for this claim is found on paragraph [0088] of the specification.

Dependent claim 9 recites that the immune cells are from a subject with a T-cell mediated inflammation disorder that is selected from the group consisting of asthma, allergic asthma, Crohn's disease, and ulcerative colitis. Support for this claim is found on paragraph [0073]-[0078] of the specification.

With respect to independent claim 13, this claim is now drawn to a method for reducing the proportion of mature dendritic cells versus immature dendritic cells in a subject comprising delivering an active agent to an immune cell of the subject having low activity or no activity of runt-related transcription 3 factor (RUNX3) gene product, wherein the active agent induces expression or over-expression of RUNX3 in the immune cells of the subject, such that the proportion of mature dendritic cells versus immature dendritic cells in the subject is reduced.

Support for this amendment is found throughout the entire specification, particularly at pages 6-7, paragraphs [0081-0085], and Examples 5-7.

New dependent claim 49 recites that the immune cells of the subject are selected from the group consisting of thymocytes and dendritic cells (DC). Support for this amendment is found in the specification, particularly at page 2, paragraphs [0022] and [0034] and page 11, paragraphs [0122] and [0123].

New dependent claim 50 recites that the active agent is selected from the group consisting of a polynucleotide encoding RUNX3 and a polynucleotide encoding a RUNX3 promoter activator. Support for this amendment is found in the specification, particularly at page 7, paragraph [0081].

New dependent claim 51 recites that the polynucleotides further comprise a viral-based vector. Support for this amendment is found in the specification, particularly on paragraphs [0086].

The presently claimed invention is based on studies using both RUNX3 knock out (KO) mouse and RUNX3 wild-type (WT) mice. Unlike the WT mice, the KO mice are homozygous for the RUNX3 null allele, wherein the wild type copy of the RUNX3 gene undergoes target disruption resulting in the prevention of the expression of the RUNX3 gene. The WT mice, on the other hand, already contain endogenous copies of the RUNX3 gene in their genome and are used in place of those mice that would have been delivered with the RUNX3 polynucleotide, as described in the specification. Accordingly, both RUNX3 WT and KO mice are employed to show the importance of RUNX3 expression in mediating T cell-mediated inhibition of inflammation.

All the data, as presented in Table 1, Examples 1-6 and Figures 1-6 are derived from the studies performed in these two types of mice. For example, as shown in Examples 1 and 2, KO mice exhibit a perturbed distribution of $CD4^+/CD8^+$ T lymphocytes and a significant increase of IL-5 level in bronchioalveolar lavage fluid whereas the WT mice do not exhibit either of those traits. Clearly, the findings regarding the increase in immune cell response as shown in KO mice enable the claimed delivery of the active agent that comprises a polynucleotide encoding RUNX3. The increase of the expression or overexpression of RUNX3 in immune cells of the

subject (having no activity or low activity of RUNX3 gene product) would, in turn, lead to the inhibition of T cell proliferation.

Additionally, as shown in Examples 5 and 6, KO mice exhibit higher levels of mature dendritic cells over immature dendritic cells, which, in turn, causes stimulation of T cell proliferation. Therefore, delivering an active agent comprising a polynucleotide encoding RUNX3 induces expression or overexpression of RUNX3 in the immune (dendritic) cells of the subject thereby inhibiting the proliferation of T cells.

Based on the foregoing and claim amendments, Applicants respectfully submit that the specification meets the enablement requirement for the claimed invention. A person skilled in the art would not need to undergo undue experimentation to practice the claimed invention without a reasonable expectation of success. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 1-9 and 13 based on 35 U.S.C. §112, first paragraph.

CONCLUSION

For at least the reasons set forth above, this application is in condition for allowance. Favorable consideration and prompt allowance of the claims are earnestly requested. Should the Examiner have any questions that would facilitate further prosecution or allowance of this application, the Examiner is invited to contact the Applicant's representative designated below.

Respectfully submitted,

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